

**ABSTRACT**

The present invention provides methods for the determination of the structure of biomolecular targets, as well as the site and nature of the interaction between ligands and biomolecular targets. The present invention also provides methods for the determination of the relative affinity of a ligand for the biomolecular target it interacts with. Also provided are methods for screening ligand or combinatorial libraries of compounds against one or more than one biological target molecules. The methods of the invention also allow determination of the relative binding affinity of combinatorial and other compounds for a biomolecular target. The present invention further provides methods for the use of mass modifying tags for screening multiple biomolecular targets. In a preferred embodiment, ligands which have great specificity and affinity for molecular interaction sites on biomolecules, especially RNA can be identified. In preferred embodiments, such identification can be made simultaneously with libraries of ligands.